REMARKS

I. Amendment to the Specification. The specification has been amended to recite subject matter concerning production of granules. Support for the amendment is found on pages 12-14 (paragraphs numbered (1), (4) and (6)) of the verified English-language translation of DE 198 49 589 that is submitted concurrently herewith. The disclosure of DE 198 49 589 is incorporated by reference at page 17, lines 8-10 of the specification. The amendment to the specification does not add new matter to the application.

II. Status of the Claims. Claims 18-34 are pending. Claims 18-34 have been amended without prejudice or disclaimer to delete the limitation of a "depot." Claim 18 has been amended further to delete the limitation of "an active ingredient combination." The aforementioned amendments do not add new matter to the application.

III. Response to Rejections. The rejections set forth in the Office Action are summarized and addressed as follows.

(i) Rejections Under 35 U.S.C. §112, first paragraph (enablement and written description).

a. Claims 1-34 are rejected for alleged lack of enablement and for alleged lack of written description, for being directed to "depot" formulations. In response, without conceding the validity of the rejections, the claims have been amended to remove the recitation that the claimed formulations are "depot" formulations. Thus, the basis of the rejections has been addressed and overcome. Withdrawal of the rejections is respectfully requested.

b. Claims 26, 27, 32 and 33 are rejected for alleged lack of written description for recitation of a medicament formulation comprising ceramic granules or calcium phosphate (claims 27 and 27) or for recitation of a bone replacement implant (claims 32 and 33). The Examiner's position is that the specification does not teach how to make such a medicament formulation or bone replacement implant and no examples have been provided. In response, it is noted that "examples are not necessary to support the adequacy of a written description...the written

description standard may be met...even when actual reduction to practice of an invention is absent." *Falkner v. Inglis,* 448 F.3d 1357, 1366 (Fed. Cir. 2006). Moreover, the specification has been amended to include subject matter incorporated by reference from DE 198 49 589. The incorporated subject matter sets forth methods for producing granules. Such granules can be used to fashion a bone replacement implant. Accordingly, without the conceding the validity of the rejection, the basis of the rejection is believed to have been addressed and overcome.

(ii) Rejections Under 35 U.S.C. §103(a). The Examiner has rejected claims 18-25 and 28-31 as allegedly obvious over Heath et al., WO 97/44015 ("Heath"). The Examiner acknowledges that Heath fails to teach the particle size rang of 20-500 μm that is called for in the instant claims. The Examiner takes the position, however, that it would have been routine optimization to obtain particles within the recited size range and that the recited size range cannot support patentability absent "unexpected or unusual results, which accrue from the instant particle sizes." The rejection is traversed on the grounds that the particles called for in the present claims have unexpected and superior properties compared to the particles disclosed in Heath.

The particle size difference between the presently claimed formulations and formulations disclosed in Heath support the patentability of the present invention, because the difference leads to unexpected and functionally significant differences in solubility, dusting and handling properties. Thus, the instant specification sets out at page 3, lines 9-15 that particles smaller than 20 μm are associated with "much dust...making direct application virtually impossible" and at page 8, lines 14-19 that smaller particles are "prone to dusting and are not free-flowing in practice, which greatly restricts accurate metering and direct application of the solid powder."

A more complete summary of the physico-chemical differences between the spray-dried microparticles disclosed in Heath and the microparticles produced in a fluidized bed (as recited in the present claims) is summarized as follows (*see* Heath at page 3, lines 19-20 and Rule 132 Declaration of Prof. Schmidt submitted on April 5, 2007 at paragraphs 5, 7-14 and Figures 1-3):

Property of microparticles	**WO 97/44015**	**Present Claims**
size	1-20 μm	20-500 μm
morphology	hollow microspheres	compact, slightly porous solid particles not having hollow-sphere characteristics
dusting	very prone to dusting	dust-free
flowability	not free-flowing	free-flowing
handling properties	difficult to handle (easily crushed), cohesive and cause problems during further processing, transport and storage	easily metered, not easily crushed and easy to spread
possibility of making combination granules containing both fibrinogen and thrombin	not possible	possible

In short, the fluidized bed drying process called for in the present claims yields microporous granules of different particle size than produced by the spray drying procedure of Heath and which have unexpected and superior characteristics compared to the granules disclosed in Heath. The unexpected, unusual results that accrue to the particle sizes recited in the claims are evidence that the claims are not obvious over Heath. For at least this reason, the present rejection should be withdrawn. Reconsideration of the claims and withdrawal of all rejections thereof under section 103 is requested.

(iii) Double Patenting. Claims 18-25, 28-31 and 34 are rejected for alleged obviousness-type double patenting over claims 1-4 and 13 of U.S. Patent No. 6,596,318 ("the '318

patent"). The rejection is traversed on the grounds that none of claims 1-4 or 13 of the '318 patent suggest the instant claims.

The analysis for an obviousness-type double patenting analysis parallels an analysis for an obviousness-rejection under section 103, with difference that the analysis is restricted to determining what is obvious from the claims of an issued patent. *See* MPEP 804, *citing In re Braithwaite,* 379 F.2d 594 (CCPA 1967), *In re Braat,* 937 F.2d 598 (Fed. Cir. 1991); and *In re Longi* 759 F.2d 887 (Fed. Cir. 1985). Thus, each limitation of the claim to be rejected must be disclosed or obvious over the claims of the issued patent. The analysis follows the factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1 (1966). MPEP 804 (Determine scope and content of patent claims relative to claim at issue in the application; determine differences between the scope and content of the patent claim and the claim at issue in the application; determine level of ordinary skill in the pertinent art; evaluate any objective indicia of nonobviousness.)

Here, the claims of the '318 patent are directed to a fibrin tissue adhesive of thrombin and fibrinogen with factor XIII in pourable solid granules. The instant claims are drawn to a formulation comprising (i) a carrier system AND (ii) an active ingredient. None of the claims of the '318 patent calls for granules including an active ingredient, as required by the instant claims. The has Examiner not set forth any finding concerning the state of the art that bears on why it would have been obvious to add an active agent to any of the formulations set forth in claims 1-4 or 13 of the '318 patent. For at least these reasons, the instant rejection should be withdrawn.

Additionally, the instant should be withdrawn because it is based on flawed explicit interpretations of the claims of the '318 patent and the law regarding obviousness-type double patenting. The Examiner asserts when the instant application was filed one of ordinary skill in the art "would have expected similar effects from the formulation of the instant claims, given the claims of [the '318 patent]. Thus, the instant claims...would have been obvious given the claims of ['318 patent]." The Examiner's assertions and conclusion are not well taken. First, the formulations claimed in the '318 patent would not have been expected to "have similar effects" as the instantly claimed formulations. As set forth above, the formulations claimed in the '318 patent lack an

"active ingredient." In the absence of an active ingredient, one of ordinary skill in the art would not expect the formulations claimed in the '318 application to "have similar effects" as the instantly claimed formulations.

Additionally, whether or not the claims of the '318 patent and the instant claims "have similar effects" is not germane to the instant obviousness-type double patenting analysis. The instant claims are directed to a biodegradable medicament formulation comprising a carrier system (as set out in claim 18 paragraph (i)) and an active ingredient. The compositions are claimed according to their constituent parts, as set out in the claims. They are not claimed according to their "effects." Moreover, there is no nexus between the "effect" of the compositions set forth in the claims of the '318 patent and any of the features set forth in paragraphs (i) and (ii) of claim 18 of the instant claims. Thus, the respective "effects" of the compositions are not germane to the instant rejection.

Lastly, in support of the present rejection, the Examiner asserts that "the scope of the '318 claims is broad enough to encompass a biodegradable blood plasma protein and an active ingredient." However, whether or not the instant claims are "encompassed" by the claims of the '318 patent is not the test for obviousness-type double patenting. The *sine quo non* for obviousness-type double patenting is whether each limitation in the pending claim is disclosed or obvious over the issued claim. There is no logical connection between the Examiner's statement that the claims of the '318 patent "do not exclude additional, unrecited elements" and a conclusion that it would be obvious to include any active ingredient to the claims of the '318 patent because there is simply no mention in the '318 patent claims (or specification) of adding any "active ingredient" to the formulations of the '318 patent. Restated, the Examiner is asserting that the instant claims are obvious because they are directed to a species that falls within the genus claimed by the '318 patent. It is well established, however, that a genus does not necessarily render obvious a species that falls within the genus. Nor has the Examiner offered any logical reason for why the "genus" of the '318 patent claims rends the "species" of the instant claims obvious. Thus, the broad claims of the '318 patent do not render the instant claims obvious. The instant rejection should thus be withdrawn.

For at least the reasons set forth above, the instant claims are not obvious over any claim of the '318 patent. Reconsideration of the claims and withdrawal of all rejections thereof for obviousness-type double patenting is respectfully requested.

IV. Conclusion. This application is believed to be in condition for allowance, which is earnestly solicited.

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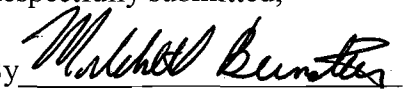
Respectfully submitted,

By 

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